

What is claimed is

1. A compound for inhibiting expression of angiogenin comprising an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin.

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2. The compound of claim 1 wherein the base sequence is configured to bind to the target portion of the nucleic acid in a manner to inhibit the expression of angiogenin.

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3. The compound of claim 2 wherein the oligonucleotide analog comprises a modified internucleotide linkage, a modified purine or pyrimidine moiety, a modified sugar moiety, a modified 5' hydroxyl moiety, a modified 3' hydroxyl moiety or a modified 2' hydroxyl moiety.

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4. The compound of claim 3 wherein the modified internucleotide linkage comprises a substituent having an improved aqueous or lipid solubility or improved resistance to nuclease digestion.

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5. The compound of claim 4 wherein the modified internucleotide linkage is selected from the group consisting of phosphorothioate, alkyl or cycloalkyl phosphorothioate, N-alkyl or cycloalkyl phosphoramidates, phosphorodithioates, alkyl or cycloalkyl phosphonates, phosphodiester, phosphotriester, C₁ - C₄ alkyl,

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cycloalkyl, short chain heteroatomic or heterocyclic backbone, morpholino backbone, polyprotein-nucleic acid or peptide-nucleic acid backbone, polyamide, $\text{CH}_2\text{-NH-O-CH}_2$, $\text{CH}_2\text{-N(CH}_3\text{)-O-CH}_2$, $\text{CH}_3\text{-O-N(CH}_3\text{)-CH}_2$, $\text{CH}_2\text{-N(CH}_3\text{)-N(CH}_3\text{)-CH}_2$ and $\text{O-N(CH}_3\text{)-CH}_2\text{-CH}_2$.

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6. The compound of claim 3 wherein the modified purine or pyrimidine moiety includes inosine.

7. The compound of claim 3 wherein the modified sugar moiety includes sugar mimetics comprising $\text{C}_4 - \text{C}_8$ cycloalkyl.

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8. The compound of claim 3 wherein the modified 5' or 3' hydroxyl moiety is selected from the group consisting of C_{1-4} alkoxy, intercalating agent, peptide, enzyme, ribozyme, substituted acridine, 2-methoxy-6-chloro-9-pentylaminoacridine, $\text{N-(6-chloro-2-methoxyacridinyl)-O-methoxydisopropylaminophosphinyl-3-aminopropanol}$ and $\text{N-(6-chloro-2-methoxyacridinyl)-O-methoxydisopropylaminophosphinyl-5-aminopentanol}$.

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9. The compound of claim 1 wherein the modified 2' hydroxyl moiety is selected from the group consisting of OH , SH , SCH_2 , OCH_3 , F , OCN , OCH_2CH_3 , OCH_2OCH_3 , $\text{OCH}_2\text{O(CH}_2\text{)}_n\text{CH}_3$, $\text{O(CH}_2\text{)}_n\text{NH}_2$ or $\text{O(CH}_2\text{)}_n\text{CH}_3$ where n is from 1 to about 10; C_1 to C_{10} lower alkyl, substituted lower alkyl, alkaryl or aralkyl; Cl ; Br ; CN ;

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CF₃, OCF₃, O, S, or N-alkyl; O, S, or N-alkenyl; SOCH₃; SO₂CH₃; ONO₂; NO₂; N₃; NH₂; heterocycloalkyl or alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a conjugate; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; and a group for improving the pharmacodynamic properties of an oligonucleotide.

10. The compound of claim 1 wherein the base sequence of the oligonucleotide or analog thereof is selected from the group consisting of

5'-GCCCATCACCATCTCTTC-3',
5'-ACACGGCATCATGAATCA-3',
5'-CCAGGGGCCCCGCTGGTTA-3',
5'-ACCAAATTTTATATTCTA-3',
5'-CAGGCCCATCACCATCAC-3',
5'-GCCCAGGCCCATCACCAT-3', and
5'-TCTCTGACACGGCATCAT-3'.

11. A composition for inhibiting expression of angiogenin comprising an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin in a pharmaceutically acceptable carrier.

12. The composition of claim 11 wherein the base sequence of the oligonucleotide or analog thereof is selected from the group consisting of

5'- GCCCATCACCATCTCTTC - 3',

5'- ACACGGCATCATGAATCA - 3',

5'-CCAGGGGCCCCGCTGGTTA-3',

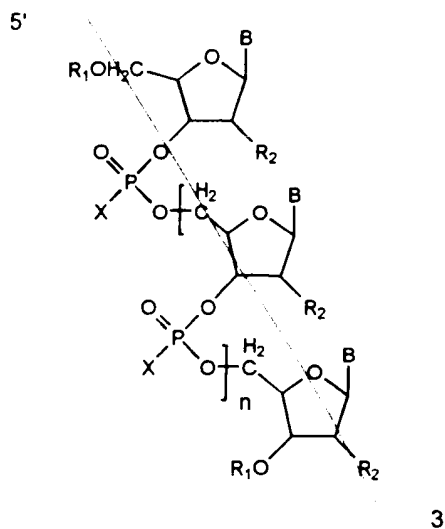
5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

13. A compound for inhibiting expression of angiogenin having the formula:



wherein

X is O, S, or C₁₋₄ alkyl;

B is adenine, guanine, cytosine, or thymine selected such that the oligonucleotide has a complementary base sequence with a portion of a target nucleic acid strand coding for angiogenin thereby inhibiting expression thereof;

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control
R₁ is H, C₁₋₄ alkyl, intercalating agent, peptide, enzyme, ribozyme, substituted acridine, 2-methoxy-6-chloro-9-pentylaminoacridine, N-(6-chloro-2-methoxyacridinyl)-O-methoxydisopropylaminophosphinyl-3-aminopropanol and N-(6-chloro-2-methoxyacridinyl)-O-methoxydisopropylaminophosphinyl-5-aminopentanol or substituted acridine;

10 R₂ is H, OH, SH, SCH₂, OCH₃, F, OCN, OCH₂CH₃, OCH₃OCH₃, OCH₃O(CH₂)_nCH₃, O(CH₂)_nNH₂ or O(CH₂)_nCH₃ where n is from 1 to about 10; C₁ to C₁₀ lower alkyl, substituted lower alkyl, alkaryl or aralkyl; Cl; Br; CN; CF₃; OCF₃; O, S, or N-alkyl; O, S, or N-alkenyl; SOCH₃; SO₂CH₃; ONO₂; NO₂; N₃; NH₂; heterocycloalkyl or alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a conjugate; a reporter group; an
15 intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; or a group for improving the pharmacodynamic properties of an oligonucleotide; and

n is 5 to 100.

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14. The compound of claim 13 wherein the base sequence is selected from the group consisting of
5'-GCCCATCACCATCTCTTC-3',

5'-ACACGGCATCATGAATCA-3',

5'-CCAGGGGCCCCGCTGGTTA-3',

5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5 5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

10 15. A method for inhibiting expression of angiogenin in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit the expression of angiogenin.

15 16. A method for reducing size of tumors associated with angiogenesis in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to reduce tumor size.

20 17. A method for decreasing production of angiogenin in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to decrease production of angiogenin.

18. A method for inhibiting metastasis of tumor cells in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit metastasis of tumor cells.

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19. A method for inhibiting the establishment of tumor cells in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit establishment of tumor cells.

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20. A method for inhibiting growth of tumors associated with angiogenesis in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit tumor growth.

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21. A method for detecting the presence of angiogenin in a sample comprising contacting the sample with a labeled oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin;

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allowing the labeled oligonucleotide or analog thereof to bind to the target portion of the nucleic acid encoding angiogenin; and

detecting the labeled oligonucleotide or analog thereof.

22. A method for detecting the presence of angiogenin in a mammal comprising administering to the mammal a labeled oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin;

5 allowing the labeled oligonucleotide or analog thereof to bind to the target portion of the nucleic acid encoding angiogenin; and
 detecting the labeled oligonucleotide or analog thereof.

23. A method for diagnosing conditions associated with abnormal
10 angiogenesis in a mammal comprising administering to the mammal a labeled oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin;

 allowing the labeled oligonucleotide or analog thereof to bind to the target portion of the nucleic acid encoding angiogenin;

15 detecting the labeled oligonucleotide or analog thereof;

 measuring the labeled oligonucleotide or analog thereof; and

 determining the abnormal condition based on the detecting and measuring of the labeled oligonucleotide or analog thereof.

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